CASE REPORT

PURPURA FULMINANS IN MENINGOCOCCAL SEPTICAEMIA IN AN ADULT: A CASE REPORT

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SUMMARY. Purpura fulminans is a rare and severe complication of meningococcal septicaemia. It presents as a petechial rash spreading rapidly in extent and depth, evolving into full-thickness skin necrosis. The condition is extremely uncommon in the adult population. We report the case of a 28-yr-old man with extensive meningococcal-related skin necrosis. The initial diagnosis was made and first treatment given in the emergency department of a local hospital, from where after 12 days he was transferred to our hospital. Our approach was based on the continuation of intensive treatment and on staged aggressive debridement. Temporary alloplastic skin grafts were used to prepare the wound bed and the wounds were closed with autologous skin grafts. The patient survived but subsequently, owing to chronic skin ulceration and scar instability, he underwent late bilateral below-the-knee amputation. The patient returned to normal deambulation with an orthopaedic prosthesis 18 months after the onset of meningococcal septicaemia.

Keywords: purpura fulminans, meningococcal septicaemia, skin necrosis, burn unit, amputation

Introduction

Purpura fulminans (PF) is a rare complication of septic shock that results in dermal and soft-tissue necrosis.

Differential diagnosis has to be made with regard to other skin diseases such as vasculitis, simple purpura, and other causes of gangrene.[1]

PF can be caused by several micro-organisms, e.g. *Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae*, group A streptococci*, Legionella pneumophila*, and viral infections.[2] Among these infections, meningococcaemia (due to *Neisseria meningitidis*) is certainly the commonest haematogenous infection known to induce PF. Five to 25% of patients with meningococcal disease (MD) develop PF.[3] This severe systemic illness now has an overall high mortality rate of 20 to 70%,[3] even if the clinical histories on the subject reported in the literature do not concern large populations. The incidence of PF from *Neisseria meningitidis* is certainly higher in children and adolescents and it is very rare in the adult population (*Table I*).[4]

Fulminant meningococcaemia first presents with high fever, chills, severe myalgia, headache, and skin and mucosal petechiae. These symptoms can progress rapidly to septic shock with multiorgan dysfunction syndrome (MODS) and a worsening of the skin conditions.[4] The disseminated spots progress to large purpuric areas deep into the skin and subcutaneous necrosis. Aggressive acute treatment, both in the critical care approach (fluid resuscitation, specific antibiotic therapy, respiratory and inotropic support) and in terms of surgery (excision and skin grafts), can improve the survival rate.[4]

Since 2002 five patients (four children and one adult) with a diagnosis of MD have been referred to our Department of Plastic and Reconstructive Surgery, Burns Centre, Traumatological Hospital, Turin, Italy. We report our experience in the management of skin infarction after meningococcal septicaemia in the sole adult patient among our cases.

Case report

A 28-yr-old previously healthy male suddenly presented high fever, initially treated with acetaminophen. The following day he had a skin rash with fast-sprouting purpuric lesions, involving especially the lower limbs. He was admitted to the emergency department of a local referral hospital with a diagnosis of suspected iatrogenic purpura.

During the first days he presented coagulative disorders with leukopenia and thrombocytopenia requiring platelet transfusions. Concurrently, antibiotic prophylaxis was started with piperacillin-tazobactam and ciprofloxacin. On day 2 his general condition deteriorated, and he presented mental confusion and nucal rigidity. A lumbar puncture was performed revealing meningococcal growth. The antibiotic therapy was then changed to penicillin (24 million units/day in continuous endovenous infusion) and rifampin (900 mg/day). The following days he presented acute respiratory failure, treated with artificial mechanical ventilation via orotracheal intubation, and severe septic shock with disseminated intravascular coagulation (DIC). Recombinant human activated protein C (rhAPC) therapy (24 g/kg/h for 4 days) was then initiated.

Extensive dermal and soft tissue necrosis (20% body surface area) developed in the meanwhile (*Fig. 1*). A confluent purpuric rash was assessed in the dorsum of the right hand and fingers, in both the extensor surfaces of the elbows, circularly in the lower legs, in all the toes, and in the soles bilaterally.

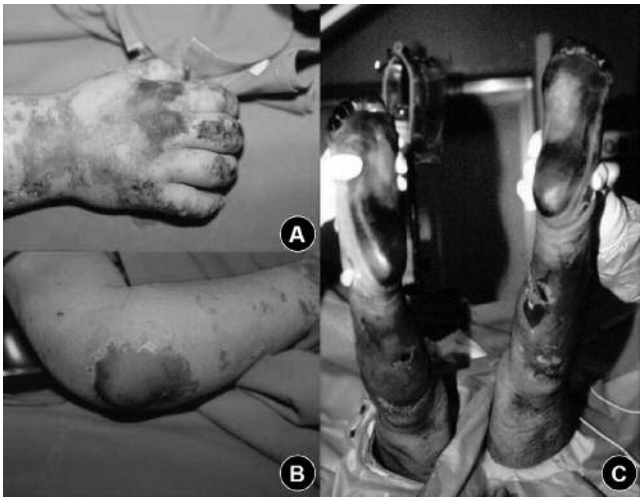

Fig. 1 - Areas of skin infarctions showing a characteristic peripheral distribution. A: confluent purpuric rash of dorsum of hand; B: full-thickness eschar of left elbow; C: extensive skin necrosis involving both legs and feet with distal digital necrosis.

On day 12 after the onset, the patient's general condition seemed to be improving and he was extubated and transferred to our hospital's intensive care unit. The following day surgical debridement of necrotic tissues at fascial level was performed on the lower limbs. The wounds were then covered with an antiseptic ointment (silver sulphadiazine cream). During dressing changes, further necrotic areas were detected (*Fig. 2A*) and on day 27 the patient returned to the operating theatre for further wound debridement and concomitant amputation of all his toes (*Fig. 2B*), together with excisions in the fascia of the right hand and both elbows. All the excised areas were covered with alloplastic glycerolized skin grafts (SG).

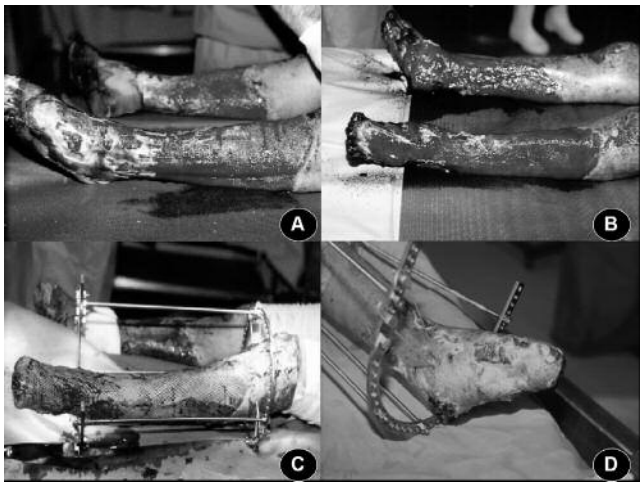

Fig. 2 - A: granulation tissue 15 days after first eschar excision, with dry gangrene in all ten toes; B: granulation tissue after three applications of allografts with necrosis of all metatarsal heads; C: skin autografts applied 35 days after first excision with concomitant set-up of Ilizarov apparatus; D: follow-up at one month.

On day 28 the patient was transferred to our Burns Unit. The wound approach was conservative and the patient underwent sequential applications of alloplastic glycerolized SG on days 31 and 35, while wound coverage with autologous SG was performed on day 47 (*Fig. 2C*). At the same time an orthopaedic surgeon applied an Ilizarov leg-ankle apparatus bilaterally to stabilize the tibio-tarsal joints (*Fig. 2C*).

One month later, further necrotic areas on both feet became demarcated (*Fig. 2D*) and the patient underwent amputation of the first and fifth metatarsus bilaterally.

Weight bearing was progressively permitted from the fourth month and the patient was discharged five months after admission with complete wound closure.

Five months later the weight-bearing surfaces presented bilateral calcaneal bone exposure (*Fig. 3A*), requiring further surgical debridement, vacuum-assisted closure therapy, and split-thickness SG.

In the following months subsequent episodes of cutaneous ulceration occurred owing to the weight bearing on the damaged bone structure of the patient's feet and to the impossibility of providing adequate soft tissue coverage. This local condition was a serious handicap for the patient which after further orthopaedic assessment led to bilateral below-the-knee amputation (*Fig. 3B*).

The patient returned to normal walking with an orthopaedic prosthesis 18 months after the initial meningococcal septicaemia (*Fig. 3C, D, E*).

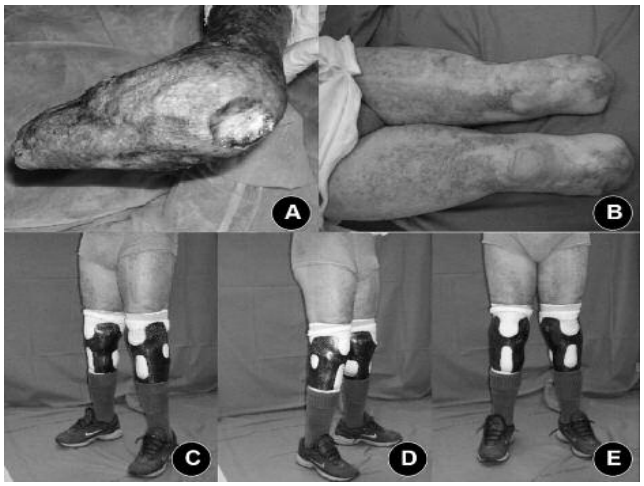

Fig. 3 - A: chronic, non-healing skin ulcer with calcaneal bone exposure due to scar instability; B: bilateral below-knee amputations; C, D, E: complete recovery from illness, with orthopaedic prosthesis for deambulation.

The patient is now able to walk without crutches and has returned successfully to his normal social and working life.

Discussion

Neisseria meningitidis colonization is very common in our population, in most cases without any clinical signs although strains of serogroups B and C sometimes have the potential to invade the bloodstream.[5] It is known that the most *Neisseria meningitidis* infections are acquired by nasopharyngeal transmission from the epithelial barrier of the nose or throat or else through the lymphoid tissue of the adenoids or tonsils.[6] Pathogenic strains have a polysaccharide capsule, which serves as a major virulence factor for the organism. Unencapsulated strains, frequently found in the nasopharynx of asymptomatic carriers, rarely cause invasive disease.[7] The incidence of meningococcal infections ranges between 0.5 and 1.5 cases per 100,000 per year - children and adolescents are however more prone to *Neisseria meningitidis* infection, which in the adult population is usually rare (*Table I*).[8]

Meningococcal infection can present as meningitis (M), M plus septicaemia, or septicaemia alone.[9] In a minority of infections, the clinical picture can be overwhelming septicaemia with endotoxic shock and DIC. *Neisseria meningitidis* reaches the peripheral tissues as an intracellular organism through the blood white cells and releases a powerful endotoxin. Meningococcal endotoxin induces oedema formation and capillary thrombosis with extravasation of blood into the interstitial space.[10] The basic physiopathological effect on the skin is DIC, characterized by specific damage to the small and medium-sized vessels of the skin, subcutaneous tissue, muscle, and bone. In this way meningococcaemia can lead to PF with a spreading petechial rash which rapidly evolves into full-thickness skin necrosis and deep muscle damage.[11]

Table I - Review of adult case series of purpura fulminans in meningococcal septicaemia

Survey	Number of patients	Age or average age (yr)
Smith et al. (1997)	2	19.27
Rintala et al. (2000)	5	Range, 17-49
Alex et al. (2004)	1	23
Schellongowski (2006)	4	Range, 17-48
Davis et al. (2007)	1	52
Alexandre et al. (2007)	1	20
Rebecca et al. (2007)	1	19
Horino et al. (2008)	1	32
Zaheed Hassan et al. (2008)	2	19 and 21
Lauren T. et al. (2009)	1	19

The extremities are the most commonly affected areas owing to their precarious perfusion. Few patients survive the acute phase of the illness even if intensive care procedures are used. The first step for correct and successful treatment is indubitably a rapid diagnosis and early commencement of a specific antibiotic therapy.

Since the inflammatory response in sepsis is procoagulant in the early stages, rhAPC, i.e. recombinant human activated protein C, an endogenous anticoagulant with anti-inflammatory properties, has recently been proposed as an emergent key drug to improve the survival rate when a clinical picture of septic shock is already present. The *Surviving Sepsis Campaign Guidelines* for the management of severe sepsis and septic shock recommend the use of rhAPC in patients with a high risk of death due to sepsis-induced organ dysfunction, identifying four such situations: acute respiratory distress syndrome; septic shock; MODS; and acute physiology and chronic health evaluation (APACHE) II $\geq$ 25.[13] Furthermore, Vincent et al. showed that rhAPC-treated adult patients with severe sepsis presenting with PF, M, MD had a lower observed 28-day mortality rate, a similar serious bleeding event rate, but a higher observed rate of intracranial haemorrhage than rhAPC-treated patients without PF, M, or MD.[14] These are surely encouraging results, although the role of rhAPC has to be confirmed in a wider range of patients.

There is very little information in the literature concerning the surgical treatment of extensive PF after MD. However, as a burns unit is an intensive care facility specializing in the treatment of extensive cutaneous wounds, it can certainly provide better patient management.[15]

Regarding local care after the first observation, the affected limbs should be carefully examined in order to prevent compartment syndrome, especially in circumferential

wounds. Debridement should be performed as soon as the patient's clinical condition becomes stable and the necrotic areas are well demarcated. Serial local re-evaluations can lead to successive debridements. In the first phase allografts and xenografts can act as a temporary physiological coverage of the wounds in the acute period in order to assure a clean and viable bed for skin autografting.[9,16] Cultured autologous keratinocytes and skin substitutes (Integra®) were used in some small series.[17,18] Skin graft failure in these cases could be due to a residual inflammatory response, continued perfusion dysfunction, or insufficient eschar excision.

The outcome of survivors is often characterized by surgical amputations of one or several extremities, despite early fasciotomies and surgical debridement of nonviable tissue. An initial conservative approach should take into consideration using different reconstructive techniques: this can reduce the level of amputation and preserve limb length, permitting a better final outcome with a more stable amputation stump. It has been suggested that bone scanning could be used or MR imaging in the acute phase in order to assess early bone viability and consequently extremity loss.[19,20] This would certainly be very useful in children because of its ability to identify areas of epiphyseal damage, predicting future limb-growth inhibition in the future, but in adults it is more difficult to make an early evaluation of the level of amputation on the basis of a single examination. For these reasons amputations are usually performed in a late phase after careful programming and preoperative assessment.

Conclusion

Purpura fulminans associated with meningococcaemia is a devastating but rare disease with high mortality.[21]

For a successful clinical approach in the acute phase, it is mandatory to make a correct diagnosis of meningococcal disease, provide life function support through advanced intensive care, and administer early specific antibiotic therapy. As to the management of septic shock and MOF, despite some promising results, the role of rhAPC continues to need better clarification.

Critical clinical conditions and a local situation similar to that of a full-thickness burn provide the rationale for treatment in a highly specialized burns centre unit. However, burns unit involvement is always secondary to the first emergency approach in the local referral hospital.

Even if this is an anecdotal case, considering the rarity of the pathology and the age of the patient, we are convinced that a conservative approach is the right choice in local wound management. This permits multiple re-evaluation of the wounds until all the nonviable tissues are excised, because early closure of the lesions is in any case quite difficult owing to poor autograft take in the acute phase of the illness.[21] Also, the later the amputation, the greater the opportunity to prepare a valid stump for a better prosthesis fit.

RÉSUMÉ. Le purpura fulminans est une complication rare et grave de la septicémie à méningocoques. La maladie se présente comme un érythème pétéchial qui se propage rapidement en ampleur et en profondeur, évoluant vers une nécrose totale de la peau. Cette condition est extrêmement rare dans la population adulte. Nous rapportons le cas d'un patient de 28 ans atteint d'une nécrose cutanée étendue d'origine méningococcale. Le diagnostic initial a été fait et le premier traitement effectué dans le service des urgences d'un hôpital local d'où, après 12 jours, le patient a été transféré dans notre hôpital. Notre approche thérapeutique se basait sur la continuation des soins intensifs et le débridement agressif par étapes. Nous avons utilisé des greffes cutanées alloplastiques temporaires pour préparer le lit de la plaie et les lésions ont été fermées avec des greffes de peau autologue. Le patient a survécu mais par la suite, à cause de l'ulcération cutanée chronique et de l'instabilité cicatricielle, il a du subir l'amputation bilatérale sous le genou. Il est retourné à la marche normale avec une prothèse orthopédique 18 mois après la première manifestation de la condition de septicémie à méningocoques.

Mots clés: purpura fulminans, septicémie à méningocoques, nécrose cutanée, unité des grands brûlés, amputation

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